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# Benzo[b]thiophen Derivatives. Part IX.<sup>1</sup> Nitration of Benzo[b]thiophen and the Isomeric Nitrobenzo[b]thiophens

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A study of the nitration of 3-nitrobenzo[b]thiophen has confirmed its lack of reactivity towards fuming nitric acid in glacial acetic acid at elevated temperatures, but has shown that substitution occurs at all positions in the benzene ring when it is treated in the cold either with a one molar proportion of potassium nitrate in concentrated sulphuric acid, or with a mixture of nitric acid, acetic acid, and acetic anhydride. The observed preference of substitution in the order 6 > 5 > 4 > 7-positions is discussed in terms of electron-density calculations for 3-nitrobenzo[b]thiophen and in terms of the influence of peri interaction in the 3,4-dinitro-compound. The <sup>1</sup>H n.m.r. spectra of 3,4-, 3,5-, 3,6-, and 3,7-dinitrobenzo[b]thiophens, the structures of which are confirmed by chemical means, and the <sup>1</sup>H n.m.r. spectra of the six isomeric mononitrobenzo [b] thiophens are recorded. Nitration of benzo [b]thiophen is shown to give some 7-nitrobenzo[b] thiophen and reassignment of structure as 3,4,6-trinitrobenzo[b]thiophen is made to a compound previously incorrectly characterised. G.I.c. retention times are recorded for the six isomeric mononitrobenzo[b]thiophens.

FEW systematic analyses of the products of electrophilic substitution in benzo[b]thiophens bearing an electron-withdrawing group in the 3-position have

<sup>1</sup> Part VIII, B. Caddy, M. Martin-Smith, R. K. Norris, S. T. Reid, and S. Sternhell, *Austral. J. Chem.*, 1968, **21**, 1853. <sup>2</sup> K. Fries, H. Heering, K. Hemmecke, and G. Siebert, Augusta 1992

Annalen, 1936, **527**, 83. <sup>3</sup> G. Van Zyl, C. J. Bredeweg, R. H. Rynbrandt, and D. C. Neckers, *Canad. J. Chem.*, 1966, **44**, 2283.

been reported <sup>2-5</sup> and the literature is conflicting in that in some cases substitution is stated to occur predominantly in the benzene ring while in others it is claimed to be confined to the thiophen ring adjacent to the *meta*-

<sup>4</sup> D. E. Boswell, J. A. Brennan, P. S. Landis, and P. G. Rodewald, *J. Heterocyclic Chem.*, 1968, **5**, 69. <sup>5</sup> Y. Matsuki and T.-C. Lee, *Nippon Kagaku Zasshi*, 1965,

**86**, 853.

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directing group. Thus, mononitration of 3-nitrobenzo-[b]thiophen (Ia) with potassium nitrate in sulphuric acid at 0-4° is reported<sup>2</sup> to give three isomeric dinitrocompounds, two of which have been identified as 3,4-dinitro-6 and 3,5-dinitro-7 benzo[b]thiophen, while

$$\begin{array}{c}
\mathbf{3} \\
\mathbf{5} \\
\mathbf{5} \\
\mathbf{5} \\
\mathbf{7} \\
\mathbf{7} \\
\mathbf{1}
\end{array}$$

$$\begin{array}{c}
\mathbf{a}; \ \mathbf{R} = \mathrm{NO}_{2} \\
\mathbf{b}; \ \mathbf{R} = -\mathrm{CO}_{2}\mathrm{H} \\
\mathbf{c}; \ \mathbf{R} = -\mathrm{CO}_{2}\mathrm{H} \\
\mathbf{c}; \ \mathbf{R} = -\mathrm{SO}_{2}\mathrm{OK} \\
\mathbf{d}; \ \mathbf{R} = \mathrm{CHO}
\end{array}$$

$$\begin{array}{c}
\mathbf{c}; \ \mathbf{R} = -\mathrm{COEt} \\
\mathbf{g}; \ \mathbf{R} = \mathrm{COPrMe} \\
\end{array}$$

the mononitration of benzo[b]thiophen-3-carboxylic acid (Ib) with fuming nitric acid in glacial acetic acid-acetic anhydride in the cold is reported <sup>3</sup> to give a mixture of the 4-, 5- and/or 7-, and 6-nitro-derivatives. Similarly, mononitration of potassium benzo[b]thiophen-3-sulphonate (Ic) with concentrated nitric acid in sulphuric acid at 70-80° is stated <sup>4</sup> to give substitution in the benzene ring, while bromination<sup>5</sup> of 3-formyl-7-methylbenzo-[b] thiophen in chloroform (but not of 3-formylbenzo-[b] thiophen (Id) which fails to react <sup>8</sup> even in the presence of a halogen carrier at 40°) has been shown to give a mixture of the 4- and 6-monobromo-derivatives. On the other hand, the carbonyl derivatives (Id)-(Ig) have been claimed <sup>9</sup> (without unequivocal proof of structure) to undergo mononitration solely in the thiophen ring when treated with fuming nitric acid and acetic acid in acetic anhydride at 0° (although treatment of 3-acetylbenzo[b]thiophen (Ie) with concentrated nitric acid in refluxing glacial acetic acid is known<sup>10</sup> to give the di-(3-benzo[b]thenoyl)-furoxan (II), and bromination of 3-nitrobenzo[b]thiophen is also stated <sup>11</sup> to give sub-



stitution in the 2-position. Bromination 12,13 or chlorination  $^{13-15}$  of 3-acetylbenzo[b]thiophen in carbon tetrachloride solution confines substitution to the side chain.

As the first stage of a detailed investigation of electrophilic substitution in 3-substituted benzo[b]thiophens designed to resolve these apparent anomalies, we report

\* Kindly supplied by Dr. P. S. Landis to permit direct comparison with their results.

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F. G. Bordwell and C. G. Albisetti, J. Amer. Chem. Soc., 1948, 70, 1955. <sup>8</sup> Y. Matsuki and T.-C. Lee, Nippon Kagaku Zasshi, 1966, 87,

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   <sup>13</sup> N. B. Chapman, K. Clarke, and B. Iddon, J. Medicin. Chem., 1966, 9, 819. <sup>14</sup> W. S. Emerson, J. Amer. Chem. Soc., 1951, 73, 1854.

our studies of the nitration of 3-nitrobenzo[b]thiophen under different conditions together with pertinent studies of the nitration of other nitrobenzo[b]thiophens. We also report investigations of the nitration of benzo-[b] thiophen itself since our findings differ in some respects from those of a recent study.<sup>4</sup>

Previous workers 3,4,16-23 have prepared 3-nitrobenzo-[b]thiophen by nitration of benzo[b]thiophen in acetic acid followed by separation of the mixed isomeric mononitrobenzo[b]thiophens from the dimeric material also formed,17,18 and fractional crystallisation or chromatographic isolation <sup>23</sup> of the preponderant 3-isomer. However, in the present work it was not found possible to establish unequivocally the purity of 3-nitrobenzo[b]thiophen prepared in this way, since independent experiments with the six pure isomeric mononitrobenzo[b]thiophens revealed them to be very difficult to separate. Thus application of t.l.c. with alumina, silica, or polyamide as adsorbent with a wide variety of solvent systems failed to give any significant differences in  $R_{\rm F}$ value between any of the six isomers. Moreover, we were unable to discover a g.l.c. system giving a unique retention time for each of the six isomers. The best resolutions obtained were with PEGA and Reoplex stationary phases supported on Chromasorb W and these could not be improved upon by employing the 12.5% polyphenyl ether supported on Diataport S\* previously used by Boswell et al.4 in the g.l.c. of nitrobenzo[b]thiophens. Temperature programming for the Reoplex columns was without effect on resolution. Only the 7-nitro-compound showed a unique retention time. The 2-, 3-, and 4-nitro-compounds showed identical retention times on all columns and mixtures of these isomers showed a single symmetrical peak. Similarly, identical retention times were shown by the 5- and 6-nitro-compounds with the retention times of all six isomers falling in the order 2-, 3-, 4- <7-<5-, and 6- as shown in Table 1.

Because of the difficulty in detecting only 2- and 4-isomers in specimens of 3-nitrobenzo[b]thiophen prepared by nitration of benzo[b]thiophen, the 3-nitrobenzo[b]thiophen (Ia) used in the present work was obtained from nitration of benzo[b]thiophen-3-carboxylic acid (Ib) as described later.<sup>24</sup> The corrected melting point of  $80-80.5^{\circ}$  for the 3-nitrobenzo[b]thiophen so obtained was higher than all previously reported melting

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 <sup>19</sup> A. W. Weston and R. J. Michaels, J. Amer. Chem. Soc., 1950, 72, 1422.

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  <sup>22</sup> N. V. Ghaisas, J. Org. Chem., 1957, 22, 703.
  <sup>23</sup> R. Zahradnik, C. Parkanyi, V. Horak, and J. Koutecky, Coll. Czech. Chem. Comm., 1963, 28, 776.
  <sup>24</sup> Ivor Brown, S. T. Reid, N. M. D. Brown, K. J. Armstrong, M. Martin-Smith, W. E. Sneader, G. C. Brophy, and S. Sternhell, to be published. to be published.

points with one exception.<sup>18</sup> The pure 4-, 6-, and 7-nitrobenzo[b]thiophens used in the chromatographic studies were obtained by decarboxylation of the corresponding 3-carboxylic acids,<sup>24</sup> and the 2-nitro-<sup>3</sup> and 5-nitro<sup>25</sup> compounds were prepared as previously described.

In connection with the preparation of 2-nitrobenzo[b]thiophen (which involves <sup>3,4</sup> the nitration of 3-bromobenzo[b]thiophen, fractional crystallisation of the relatively insoluble 3-bromo-2-nitrobenzo[b]thiophen, and debromination of the purified 3-bromo-2-nitro- compound) we found that the composition of the mixed products obtained on the nitration of the 3-bromobenzo-[b]thiophen is highly dependent upon the conditions employed. Thus, treatment of 3-bromobenzo[b]thiophen with fuming nitric acid in glacial acetic acid and acetic anhydride at 5-10° as previously used by Van Zyl *et al.*<sup>3</sup> afforded, in our hands, a mixture of four products,<sup>26</sup> whereas nitration by means of 90% nitric View Article Online

g.l.c. traces, it can be concluded that both methods for the nitration of benzo[b]thiophen give essentially similar isomer distributions.

In view of the inapplicability of g.l.c. as a method of complete analysis for mixtures of mononitrobenzo[b]-thiophens, the mixture resulting from the reaction of nitric acid in acetic acid on benzo[b]thiophen at 60° was analysed quantitatively by <sup>1</sup>H n.m.r. spectroscopy as described in the Experimental section. The results indicated the complete absence of the 5-nitro-isomer in accord with earlier <sup>3,4</sup> refutations of a claim <sup>23</sup> for the presence of this compound, and gave the approximate proportions of the 3-, 4-, 2-, 7-, and 6-nitrobenzo[b]-thiophen present as 56:13:12:11:10. These figures appear to exaggerate the amount of the 7-nitro-compound but otherwise are in fair agreement with the g.l.c. results which indicate a ratio of 87:5:8 for the 2- plus 3- plus 4-nitro-compounds to the 7-nitro-compound to the

TABLE	1
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G.l.c. retention times \* of the six isomeric nitrobenzo[b]thiophens under different conditions

	Position of nitro-group					
Stationary phase, column length, temperature, gas flow (Ar)	2-	3-	4-	5-	6-	7-
12.5% Polyphenyl ether (6 ring), 4 ft., 187°, 130 ml./min	$2167.5 \\ (18.25)$	$2167.5 \\ (18.25)$	$2167.5 \\ (18.25)$	$2209.7 \\ (22.0)$	2209.7 (22.0)	2187.7 (20.0)
10% PEGA, 5 ft., 200°, 45 ml./min	$2783 \cdot 1$ (19 $\cdot$ 3)	$2783 \cdot 1 \\ (19 \cdot 3)$	$2783 \cdot 1$ (19·3)	$2877 \cdot 0 \\ (26 \cdot 1)$	$2877.0 \\ (26.1)$	$2826 \cdot 1$ (21.8)
3% Versamide, 4 ft., 187°, 130 ml./min	$2155.0 \\ (7.75)$	$2155.0 \ (7.75)$	2155.0 (7.75)	$2217 \cdot 5 \\ (9 \cdot 5)$	$2217.5 \\ (9.5)$	$2188.0 \\ (8.75)$
10% Reoplex, 6 ft., 200°, 45 ml./min	$2251 \cdot 2$ (18 $\cdot$ 0)	$2251 \cdot 2$ (18 $\cdot$ 0)	$2251 \cdot 2$ (18 $\cdot$ 0)	$2317 \cdot 7$ (23 $\cdot 5$ )	$2317.7 \\ (23.5)$	$2284.7 \\ (21.0)$
10% Reoplex, 6 ft., 100-200, † 45 ml./min.)	(33.5)	(33.5)	(33.5)	(39.5)	(39.5)	(36.5)

\* The main entries shown are values expressed according to the Kováts Retention Index System as described by L. S. Ettre, Analyt. Chem., 1964, 36, 31A. Numbers in brackets are retention times in minutes.  $\dagger$  Temperature programmed 100° for 5 min., then 10°/min. to 200°.

acid in acetic acid at  $15-20^{\circ}$  as employed by Boswell *et al.*<sup>4</sup> afforded, in addition to unchanged 3-bromobenzo-[b]thiophen, only the previously identified <sup>4</sup> 3-bromo-2-nitro- and 3-bromo-4-nitro-benzo[b]thiophen.

G.l.c. analysis of different fractions obtained from the products of benzo[b]thiophen with nitric acid in acetic acid gave unequivocal evidence of the presence of small amounts of the previously 3,4,16-23 undetected 7-nitrobenzo[b]thiophen. Moreover, g.l.c. analysis of the total products obtained from the nitration of benzo[b]thiophen with nitric acid in acetic acid-acetic anhydride at 0° revealed the relative areas under the three peaks corresponding respectively to the 2- and/or 3- and/or 4-isomers, the 7-isomer, and the 5- and/or 6-isomers, to be similar to those of the total product from the nitric acid-acetic acid procedure, although the method involving the acetic anhydride gave appreciable quantities of unchanged benzo[b]thiophen unless an excess of nitric acid was employed. Since synthetic mixtures of 4-nitrobenzo[b]thiophen, 6-nitrobenzo[b]thiophen, and 7-nitrobenzo[b] thiophen of known composition gave the correct analysis to  $\pm 5\%$  on integration of the areas under the

<sup>25</sup> L. F. Fieser and R. G. Kennelly, J. Amer. Chem. Soc., 1935, 57, 1611.
<sup>26</sup> K. J. Armstrong and M. Martin-Smith, to be published.

6-nitro-compound. They also stand in reasonable agreement with previous analyses of the mixed product resulting from the treatment of benzo[b]thiophen with nitric acid in acetic acid, using i.r. spectroscopy,<sup>3</sup> or g.l.c.<sup>3,4</sup> of the derived mixture of 2-phenylethylamine and isomeric ethylanilines produced by reduction of the nitro-group followed by Raney-nickel desulphurisation, if allowance is made for the failure to detect the 7-nitro-compound as *m*-ethylaniline in the second procedure and its failure to reveal the 3-nitro-compound as 1-phenylethylamine.

A further point emerging from our g.l.c. studies of the isomeric mononitrobenzo[b]thiophens and our inability to resolve mixtures of the 5- and 6-isomers concerns the purity of the substance reported <sup>4</sup> as 6-nitrobenzo[b]-thiophen. This was obtained <sup>4</sup> by nitration of the potassium salt of benzo[b]thiophen-3-sulphonic acid contaminated with the 2-isomer, followed by passage of steam at 150—180° through the diluted reaction mixture to give, in the distillate, a mixture of mononitrobenzo[b]-thiophens, which was then subjected to preparative g.l.c.; the material corresponding to the major peak was collected as 6-nitrobenzo[b]-thiophen. In view of our demonstration that, in addition to undergoing nitration in the 3-position with displacement of the

carboxy group, benzo[b]thiophen-3-carboxylic acid,24 like 3-nitrobenzo[b]thiophen as reported in the present paper, undergoes mononitration in the 4-, 5-, 6-, and 7-positions, it might be expected by analogy that potassium benzo[b]thiophen-3-sulphonate would also yield some 5-nitrobenzo[b]thiophen. That the material earlier reported  $^{4}$  as 6-nitrobenzo[b]thiophen could indeed be a mixture of the 5- and 6-isomers is suggested by its recorded melting point of 95-97° since we found that although pure 6-nitrobenzo[b]thiophen prepared by decarboxylation of 6-nitrobenzo[b]thiophen-3-carboxylic acid had a melting point of 79-80°, synthetic mixtures of the 5- and 6-isomers showed elevated melting points; a 1:1 mixture, for example, melting at 93—110°, and a 3:1 mixture melting at 100-130°. Other mixtures of pairs of isomeric nitrobenzo[b]thiophens showed normal melting-point depressions. As a further comparison between our specimen of 6-nitrobenzo[b]thiophen and the previously reported material<sup>4</sup> we measured its <sup>1</sup>H n.m.r. spectrum in 3% deuteriobenzene. The results, as shown in Table 3, are fully in accord with the assigned structure, but differ considerably from the parameters recorded <sup>4</sup> by the American workers.

Attempted mononitration of benzo[b]thiophen with a molar proportion of potassium nitrate in concentrated sulphuric acid at  $0-4^{\circ}$  gave very little mononitrated material. In addition to large quantities of polymeric material and unchanged benzo[b]thiophen, the identifiable products formed in low yield were mainly dinitroand trinitro-compounds. No evidence was found for the formation of the dimeric material formed under other conditions of nitration.<sup>17,18</sup> Similarly, treatment of benzo[b]thiophen with a two molar proportion of potassium nitrate in cold sulphuric acid gave mainly polymeric material with small quantities of other compounds of which 3,4,6-trinitrobenzo[b]thiophen was positively identified.

Attempted nitration of 3-nitrobenzo[b]thiophen with fuming nitric acid in glacial acetic acid at 105° confirmed the earlier report<sup>3</sup> that no reaction occurs under these conditions. Treatment of 3-nitrobenzo[b]thiophen with a molar proportion of potassium nitrate in concentrated sulphuric acid at  $0-4^{\circ}$  as described by Fries *et al.*<sup>2</sup>, in our hands, gave smooth conversion into a mixture of five products, rather than three as previously reported,<sup>2,4</sup> in addition to small amounts of polymeric material and unchanged starting material. Column chromatography over silica gel monitored by t.l.c. afforded all five products in pure form. Four of the products were shown to be dinitrobenzo[b]thiophens by mass spectrometry and were readily assigned unequivocal structures by <sup>1</sup>H n.m.r. spectroscopy (see below), as had been anticipated at the time of our <sup>1</sup>H n.m.r. spectroscopic survey of subbenzo[b]thiophens.<sup>1</sup> The structures stituted thus assigned were confirmed by chemical means.

Starting material was eluted first followed by 3,7-dinitrobenzo[b]thiophen (III), as shown by its identity with a specimen prepared by the mononitration of 7-nitrobenzo[b]thiophen. The third compound eluted was shown to be 3,6-dinitrobenzo[b]thiophen (IV) in a similar way and the fourth compound was identified as 3,5-dinitrobenzo[b]thiophen (V) by direct comparison with the products of mononitration of 6-nitrobenzo[b]-thiophen and 5-nitrobenzo[b]thiophen, respectively.



These results thus confirm the conclusion of Bordwell and Albisetti,<sup>7</sup> made on the grounds of identity of m.p. but apparently without direct comparison of specimens, that the dinitro-compound C of Fries *et al.*<sup>2</sup> is, in fact, **3**,5-dinitrobenzo[b]thiophen. The fifth compound to be eluted was **3**,4-dinitrobenzo[b]thiophen (VI) (compound A of Fries *et al.*<sup>2</sup>) and was converted without difficulty (*cf.* ref. 4) into 4-nitrobenzo[b]thiophen <sup>2,6,21</sup> by means of ethanolic ammonia and hydrogen sulphide. None of the four dinitrobenzo[b]thiophens thus obtained corresponded to the dimorphic ' compound B' of Fries *et al.*<sup>2</sup> and since all had much higher m.p.'s it must be concluded that their ' compound B' was a mixture.

The sixth compound to be eluted proved, on mass spectrometric examination, to be a trinitrobenzo[b]thiophen and it was found to be identical with the identical further nitration products obtained from both 3,6-dinitrobenzo b thiophen (IV) and 3,4-dinitrobenzo b thiophen (VI), but different from the identical further nitration products obtained from both 3,5-dinitrobenzo-[b]thiophen (V) and 3,7-dinitrobenzo[b]thiophen (III). Accordingly this compound, which was also identical with the major well-defined product resulting from the treatment of 3-nitrobenzo[b]thiophen with a two molar proportion of potassium nitrate in concentrated sulphuric acid at  $0-4^{\circ}$ , must be assigned the structure 3.4.6-trinitrobenzo[b]thiophen (VII). Previous assignments of structure as the 3,4,7-trinitro-<sup>2</sup> or the 3,5,7-trinitro-7 compound must accordingly be revoked.

G.l.c. analysis of the total product obtained from the nitration of 3-nitrobenzo[b]thiophen with a molar proportion of potassium nitrate in concentrated sulphuric acid revealed well defined separations of all four dinitrobenzo[b]thiophens. Integration of the areas under the g.l.c. trace revealed the ratio of the 3,6-, 3,5-, 3,4-, and 3,7-dinitrobenzo[b]thiophens in the mixture to be 37:23:19:7 and a similar isomer distribution was found in the product resulting from the treatment of 3-nitrobenzo[b]thiophen with fuming nitric acid in an acetic acid-acetic anhydride mixture at  $0-4^{\circ}$ . Independent measurements with known mixtures of authentic

dinitro-compounds revealed the method to be accurate to  $\pm 5\%$ . Despite the well recognised shortcomings in the application of electron density calculations based on ground states to the prediction of chemical reactivities,

3- and 4-positions which is undoubtedly present in the benzo[b]thiophen series, as evidenced, for example, by the different courses taken by the nitration of 4-bromo-5-hydroxybenzo[b]thiophen and 3,4-dibromo-5-hydroxy-

### TABLE 2

100 MHz <sup>1</sup>H n.m.r. data of 3,X-dinitrobenzo[b]thiophens as measured in CDCl<sub>3</sub> solutions

Compound	Conc. in $CDCl_3$ (w/v)	Chemical shifts in p.p.m. (to $\pm 0.01$ p.p.m.)	Coupling constants (Hz) (to $\pm 0.1$ Hz unless otherwise indicated)
(III)	4	2-H = 8.88, 4-H = 9.02, 5-H = 7.83, 6-H = 8.56	$J_{4.5}$ 8.0, $J_{5.6}$ 8.1, $J_{4.6}$ 1.0, $J_{2.6}$ 0.45 $\pm$ 0.05
(IV)	6	2-H = 9.00, 4-H = 8.79, 5-H = 8.46, 7-H = 8.85	$J_{4,5}$ 9.4, $J_{5,7}$ 2.1, $J_{4,7}$ 0.7
(V)	3.5	2-H = $8\cdot89$ , 4-H = $9\cdot49$ , 6-H = $8\cdot38$ , 7-H = $8\cdot06$	$J_{6,7} \begin{array}{c} 9\cdot 2, \ J_{4,6} \ 2\cdot 3, \ J_{4\cdot 7} \ 0\cdot 6, \ J_{2,6} \ 0\cdot 5 \ \pm \ 0\cdot 05, \ J_{2,4} \  eq 0 \ * \end{array}$
(VI)	2	2-H = 8.60, 5-H = 8.09 or 8.15, 6-H = 7.65, 7-H = 8.15 or 8.09	$J_{5,6}$ 8.0, $J_{6,7}$ 8.0, $J_{5,7}$ 1.0, $J_{2,6}$ 0.4 $\pm$ 0.05

\* By decoupling.

#### TABLE 3

100 MHz <sup>1</sup>H n.m.r. data for the isomeric mononitrobenzo[b]thiophens in CDCl<sub>3</sub>

	Conc. in CDCl <sub>2</sub>		
Compound	(w/v)	Chemical shifts in (p.p.m.) *	Coupling constants (Hz) †
2-Nitrobenzo[b]thiophen ‡	10	3-H = 8·148 ± 0·0002, 4-H = 7·886 ± 0·0002, 5-H = 7·463 ± 0·0003, 6-H = 7·545 ± 0·0003, 7-H 7·792 ± 0·0002	$\begin{array}{c} J_{4.5} \ 8.14 \pm 0.03, \ J_{5.6} \ 7.24 \pm 0.03, \\ J_{6.7} \ 8.30 \pm 0.04, \ J_{4.6} \ 1.22 \pm 0.03, \\ J_{5.7} \ 1.10 \pm 0.04, \ J_{4.7} \ 0.75 \pm 0.03, \\ J_{3.7} \ 0.92 \pm 0.03, \ J_{3.4} \ 0.44 \pm 0.03, \\ J_{3.6} \ 0.06 \pm 0.03, \ J_{3.5} \ 0.02 \pm 0.03 \end{array}$
3-Nitrobenzo[b]thiophen ‡	5	$\begin{array}{l} \text{2-H} = 8{\cdot}62, \ \text{4-H} = 8{\cdot}539 \pm 0{\cdot}0003, \\ \text{5-H} = 7{\cdot}548 \pm 0{\cdot}0003, \ \text{6-H} = 7{\cdot}462 \pm 0{\cdot}0004, \\ \text{7-H} = 7{\cdot}829 \pm 0{\cdot}0002 \end{array}$	$\begin{array}{c} J_{4.5} \ 8.35 \pm 0.05, \ J_{5.6} \ 7.19 \pm 0.04, \\ J_{6.7} \ 8.26 \pm 0.05, \ J_{4.6} \ 1.20 \pm 0.05, \\ J_{5.7} \ 1.15 \pm 0.04, \ J_{4.7} \ 0.85 \pm 0.03, \\ J_{2.6} \ 0.50 \pm 0.05 \end{array}$
4-Nitrobenzo[b]thiophen	6	2-H = 7.76, $3-H = 8.21$ , $5-H = 8.33$ , 6-H = 7.45, $7-H = 8.16$	$\begin{array}{c} J_{2,3} 5 \cdot 8, \ J_{5,6} 8 \cdot 0, \ J_{6,7} 8 \cdot 2, \ J_{5,7} 1 \cdot 0, \\ J_{3,7} 0 \cdot 9, \ J_{2,6} 0 \cdot 5 \end{array}$
5-Nitrobenzo[b]thiophen	4	2-H = 7.67, 3-H = 7.48, 4-H = 8.70, 6-H = 8.19, 7-H = 7.97	$\begin{array}{c} J_{2,3} \ 5 \cdot 6, \ J_{6,7} \ 8 \cdot 9, \ J_{4,6} \ 2 \cdot 1, \\ J_{4,7} \approx 0 \cdot 6, \ J_{3,7} \approx 0 \cdot 7, \ J_{2,6} \ 0 \cdot 3 \end{array}$
6-Nitrobenzo[b]thiophen	3	2-H = 7.80, 3-H = 7.45, 4-H = 7.91, 5-H = 8.22, 7-H = 8.80	$J_{2,3} \begin{array}{c} 5 \cdot 5, \ J_{4,5} \\ J_{3,7} \end{array} 8 \cdot 9, \ J_{5,7} \begin{array}{c} 2 \cdot 15, \ J_{4,7} \end{array} 0 \cdot 5, \ J_{3,7} \end{array}$
6-Nitrobenzo[ $b$ ]thiophen ¶	$3\%$ in $C_6D_6$	$\begin{array}{l} 2\text{-}\mathrm{H}=6\text{\cdot}90,\ 3\text{-}\mathrm{H}=6\text{\cdot}68,\ 4\text{-}\mathrm{H}=7\text{\cdot}09,\\ 5\text{-}\mathrm{H}=7\text{\cdot}86,\ 7\text{-}\mathrm{H}=8\text{\cdot}27 \end{array}$	$\begin{array}{c} J_{2,3} 5 \cdot 5, \ J_{4,5} 8 \cdot 9, \ J_{5,7} 2 \cdot 1, \ J_{4,7} 0 \cdot 5, \\ J_{3,7} 0 \cdot 8, \ J_{3,4} 0 \cdot 3, \ J_{2,5} \text{ or } J_{3,5} \leqslant 0 \cdot 15 \end{array}$
7-Nitrobenzo[b]thiophen	2	2-H = 7.66, 3-H = 7.48, 4-H = 8.14, 5-H = 7.53, 6-H = 8.40	$J_{2,3} \stackrel{5}{_{-5}} 5.5, J_{4,5} \stackrel{8}{_{-0}} 8.0, J_{5,6} \stackrel{8}{_{-0}} 8.0, J_{4,6} \stackrel{1}{_{-0}} 1.0, J_{5,6} \stackrel{1}{_{-0}} 3.0 \stackrel{1}{_{-0}} 5.0 \stackrel{1}{_{-0}} 1.0$

\* To  $\pm 0.01$  p.p.m. unless otherwise indicated.  $\dagger$  To  $\pm 0.1$  Hz unless otherwise indicated.  $\ddagger$  Analysed by iterative procedure (see Experimental section). ¶ Spectrum measured in  $C_6 \overline{D}_6$  to permit direct comparison with data reported by Boswell *et al.*<sup>4</sup>

and their previous indifferent success in the prediction of substitution patterns in the benzo[b]thiophen series 5,23,27-29 an attempt to rationalise the product ratio was made by performing an LCAO-MO Hückel calculation \* on 3-nitrobenzo[b]thiophen treated as a 14  $\pi$ -electron system where the nitro-group and sulphur atom (the  $pd^2$ -hybrid model was used) contribute four and two electrons respectively. The heteroatom coulomb (h) and bond (k) integrals were as follows <sup>30</sup>:  $h_{\rm N} =$ 2.2,  $h_0 = 1.4$ ,  $h_8 = -0.1$ ;  $k_{N-0} = 1.67$ ,  $k_{C-N} = 1.2$ ,  $k_{C-S} = 0.8$  and  $k_{S-S'} = 1$ —all in units of  $\beta$ . The results as summarised in formula (VIII) would indicate a theoretical preference for electrophilic substitution in the positional order 4 > 6 > 5 > 7. Considering the pronounced 'peri' interaction between substituents in the

\* The secular determinant was diagonalised using a Hückel programme based on Jacobi's method on a KDF9 computer.

 K. Kikuchi, Sci. Rept. Tohoku Univ., 1957, 41, No. 1, 35.
 Y. Matsuki and T. Kanda, Nippon Kagaku Zasshi, 1965, 86, 637.

benzo[b]thiophen,<sup>31</sup> and which would be expected to inhibit formation of the 3,4-dinitro-isomer, the observed



order of preference of substitution in positions 6 > 5 >4 > 7, which simply involves a displacement down the

<sup>29</sup> Y. Matsuki and F. Shoji, Nippon Kagaku Zasshi, 1965, 86, 1067.

<sup>&</sup>lt;sup>30</sup> P. H. Rieger and G. K. Fraenkel, J. Chem. Phys., 1963, 39, 609; A. Streitweiser, jun., 'Molecular Orbital Theory for Organic Chemists,' Wiley and Sons, Inc., New York, 1961, p. 126.
<sup>31</sup> M. Martin-Smith and S. T. Reid, J. Chem. Soc., 1960, 938.

order for position 4, can thus be seen to be in reasonable agreement.

Org.

The 100 MHz <sup>1</sup>H n.m.r. data of compounds (III)—(VI) are shown in Table 2. As anticipated from our earlier studies,<sup>1</sup> the <sup>1</sup>H n.m.r. spectra of these 3,X-disubstituted benzo[b]thiophens (where  $X \neq 2$ ) can be regarded as arising from 3-spin systems due to protons on the benzene rings, with cross-ring coupling due to 2-H as a first-order perturbation. The well known relative magnitudes of  $J_o$ ,  $J_m$ , and  $J_p$  permit instant identification of (III) and (VI) as '1,2,3-trisubstituted benzenes' and of (IV) and



FIGURE 1 100 MHz <sup>1</sup>H n.m.r. spectrum of 2-nitrobenzo[b]thiophen [10% (w/v) in CDCl<sub>3</sub>]. The computed spectrum corresponds to the output of the programme LAOCN 3 (see Experimental section) and the parameters listed in entry 1 in Table 3. Lines in the computed spectrum which appear less than 0.05 Hz apart are summed. Features marked 'Imp.' are assigned to impurities

(V) as '1,2,4-trisubstituted benzenes'. The established<sup>1</sup> coupling between 2-H and 6-H permitted ready distinction between structures (IV) and (V) and between structures (III) and (VI), while the extreme downfield shift of 4-H in (V), ascribable to a combination of *ortho*-to-nitro- and *peri* effects (see below), further distinguishes compounds (IV) and (V). We attribute the relatively high chemical-shifts in (VI) as compared to (IV), an effect which is especially obvious in the directly comparable data for 2-H, to the mutual buttressing of the two nitro-groups in (VI) with the consequent diminution of deshielding effects due to both magnetic anisotropy of the nitro-groups <sup>32</sup> and steric suppression of ground-state mesomeric effects.

Table 3 records the 100 MHz <sup>1</sup>H n.m.r. data for the six <sup>32</sup> P. R. Wells Austral. I. Chem. 1964 **17** 967

<sup>32</sup> P. R. Wells, Austral. J. Chem., 1964, 17, 967.
 <sup>33</sup> N. B. Chapman, D. F. Ewing, R. M. Scrowston, and R. Westwood, J. Chem. Soc. (C), 1968, 764.

isomeric mononitrobenzo[b]thiophens measured in deuteriochloroform solution thus permitting direct comparison with the results obtained in previous surveys <sup>1,33</sup> of compounds belonging to the benzo[b]thiophen series.



FIGURE 2 100 MHz <sup>1</sup>H n.m.r. spectrum of 3-nitrobenzo[b]thiophen [5% (w/v) in  $\text{CDCl}_3$ ]. The computed spectrum corresponds to the output of the programme LAOCN 3 (see Experimental section) and the parameters listed in entry 2 in Table 3. Lines in the computed spectrum which appear less than 0.05 Hz apart are summed. Features marked with asterisks are lines which have the splitting due to 2-H superimposed as a first-order perturbation (see Experimental section)

Published data,<sup>4</sup> showing several erroneous values for coupling constants, on the <sup>1</sup>H n.m.r. spectra of the mononitrobenzo[b]thiophens were obtained from measurements in deuterioacetone or deuteriobenzene and so are not amenable to comparative studies.

The <sup>1</sup>H n.m.r. spectral characteristics of 2-nitrobenzo-[b]thiophen and 3-nitrobenzo[b]thiophen, as summarised in Table 3, were obtained by an iterative procedure as described in the Experimental section and the computed spectra, which are in excellent agreement with the experimental spectra, are shown in Figures 1 and 2, respectively.

Analysis of the chemical shifts in the isomeric mononitrobenzo[b]thiophens in terms of downfield shifts with respect to the signals from the corresponding protons in benzo[b]thiophen itself reveals that an ortho-relationship to the nitro-group gives a shift of 0.81—1.19 p.p.m., a meta-relationship gives a shift of 0.09—0.19 p.p.m., a *para*-relationship gives a shift of 0.28—0.32 p.p.m., and a *peri*-relationship gives a shift of 0.72—0.88 p.p.m. Individual values are shown in Table 4. The corresponding values as between nitrobenzene and benzene<sup>34</sup> are ortho 0.95, meta 0.17, and para 0.33 p.p.m. The *peri*effect of the nitro-group at C-1 on 8-H in naphthalene<sup>32</sup> is 0.79 p.p.m. The largest downfield shifts caused by the nitro-groups at more remote positions (last column  $\mu A$ . I.r. spectra were obtained on a Perkin-Elmer 157 spectrophotometer in Nujol mull or in KCl disc.

Column chromatography, unless otherwise stated, was carried out with 'Silica Gel for Chromatography '(May and Baker Ltd., Dagenham, England) with ca. 25 g. of silica to 1 g. of crude product. The columns were eluted first with light petroleum (b.p. 60—80°) then increasing in 10% increments to 100% benzene. The t.l.c. plates were made up with Silica Gel G (E. Merck AG, Darmstadt, Germany) 30 g. in 60 ml. of water, spread to a thickness of 0.25 mm. and dried in an oven at 115° for 1 hr. They were run in a tank containing chloroform-benzene (1:1) and developed in an iodine tank.

<sup>1</sup>H N.m.r. Spectroscopy.—Spectra were obtained in 2-10% (w/v) CDCl<sub>3</sub> solution on a Varian HA 100 n.m.r. spectrometer.

The three-spin systems in the spectra of the 4-, 5-, 6-, and 7-nitrobenzo[b]thiophens and of the dinitro-derivatives (III)—(VI) were analysed by using the ABX approximation. Consideration of the actual magnitudes of chemical shifts and coupling constants (Tables 2 and 3) showed, however, that all the  $\Delta \nu/J$  values at 100 MHz are so large that no significant error is introduced by taking the experi-

TABLE 4

Downfield shifts of the proton signals in mononitrobenzo[b] thiophens relative to their chemical shifts in benzo[b] thiophen \* (p.p.m.)

	Downfield shifts s	hown accord	ing to the re	lative positi	ons of the proton and the nitro-group
Compound	ortho	meta	para	peri	Others
2-Nitrobenzo[b]thiophen	3-H 0.81				4-H 0.07, 5-H 0.10, 6-H 0.22, 7-H -0.09
3-Nitrobenzo[b]thiophen	2-H 1·19			4-H 0·72	5-H 0·19, 6-H 0·12, 7-H -0·05
4-Nitrobenzo[b]thiophen	5-H 0·97	6-H 0·11	7-H 0·28	3-H 0.88	2-H 0·33
5-Nitrobenzo[b]thiophen	4-H 0.88, 6-H 0.85	7-H 0·09			2-H 0·24, 3-H 0·15
6-Nitrobenzo[b]thiophen	5-H 0·86, 7-H 0·92	4-H 0.09			2-H 0·37, 3-H 0·12
7-Nitrobenzo[b]thiophen	6-H 1.06	5-H 0·19	4-H 0·32		2-H 0·23, 3-H 0·15

\* The chemical shifts in benzo[b]thiophen were taken from the data for 5-deuteriobenzo[b]thiophen,<sup>1</sup> with the exception of the chemical shift of 5-H which was derived from the data of Chapman *et al.*<sup>33</sup> As the chemical shifts of all remaining protons in ref. 33 appear to lie between 0.02 and 0.04 p.p.m. upfield of the corresponding values in ref. 1 (presumably due to a small concentration effect), we have added 0.03 p.p.m. to the chemical shift of 5-H thus accepting the value of 7.36 p.p.m.

in Table 4) are those for 2-H in 4-nitrobenzo[b]thiophen and 6-nitrobenzo[b]thiophen. We consider it significant that favourable resonance forms can be drawn placing a positive charge at C-2 in both compounds.

Examination of the vicinal coupling constants in 2-nitrobenzo[b]thiophen and 3-nitrobenzo[b]thiophen (column 4, Table 3) shows that  $J_{4.5}$  and  $J_{6.7}$  are larger than  $J_{5.6}$ . This effect is undoubtedly due to partial bond fixation <sup>35</sup> which is reflected in other <sup>1</sup>H n.m.r. data.<sup>1,33</sup> The results of iterative analysis of the <sup>1</sup>H n.m.r. spectrum of 2-nitrobenzo[b]thiophen (first entry, Table 3) confirm the existence of previously postulated <sup>1</sup> non-negligible long-range coupling between 3-H and 4-H.

## EXPERIMENTAL

All m.p.s were determined on a Gallenkamp melting-point apparatus and are corrected. Mass spectra were determined with an A.E.I. M.S.9 double-focusing mass spectrometer with a solid insertion probe. Spectra were run at 8 kv. The electron beam was 70 ev and the trap current was 100

<sup>34</sup> H. Spiesecke and W. G. Schneider, J. Chem. Phys., 1961, **85**, 731; F. Langenbucher, R. Mecke, and E. D. Schmid, Ann. Chem., 1963, **669**, 11, J. Chem. Phys., 1963, **39**, 1901. mental values of the appropriate splittings as direct measures of coupling constants.

The <sup>1</sup>H n.m.r. spectrum of 2-nitrobenzo[b]thiophen was analysed by the method of Bothner-By and Castellano <sup>36</sup> (LAOCN 3) as a five-spin system. The errors quoted in entry 1, Table 3, are taken directly from the computer output. The root mean square error at the final iteration was 0.094 Hz. Of the 94 lines which were of sufficient intensity to appear in the final computer output, all but 13 were measured in the spectrum, although in several cases more than one theoretical line had to be assigned to a single measured frequency due to insufficient resolution. The largest deviation of any single line was 0.24 Hz (one case), which was considered satisfactory as the accuracy of the experimental line measurements was no better than  $\pm 0.05$ Hz. The excellent fit of the computed and experimental spectrum can be seen in Figure 1.

The <sup>1</sup>H n.m.r. spectrum of 3-nitrobenzo[b]thiophen was analysed in the same manner <sup>36</sup> but as a four-spin system, the interaction of 2-H with 6-H being superimposed as a first-order perturbation. The root mean square error at the

<sup>&</sup>lt;sup>35</sup> S. Sternhell, Quart. Rev., 1969, 23, 236.

<sup>&</sup>lt;sup>36</sup> A. A. Bothner-By and S. Castellano, J. Chem. Phys., 1964, **41**, 3863.

final iteration was 0.087 Hz. Out of the 37 lines which were of sufficient intensity to appear in the final computer output, all but 4 were measured in the spectrum, and in only very few cases (Figure 2) more than one theoretical line had to be assigned to a single measured frequency due to insufficient resolution. The fit of the individual lines and the accuracy of measurements were comparable to those obtained with the spectrum of 2-nitrobenzo[b]thiophen, and the satisfactory correspondence between the computed and experimental spectra may be seen in Figure 2.

The analysis of the mixture of mononitrobenzo[b]thiophens resulting from the action of nitric acid in acetic acid on benzo[b] thiophen at 60° (see text) was performed in the following manner. The spectra of a 10% (w/v) solution in CDCl<sub>3</sub> at 60° and of a ca. 2% (w/v) solution in CDCl<sub>3</sub> at  $28^{\circ}$  (standard probe temperature) were compared and were found to be identical from the point of view of the subdivision into groups of signals (see below). The spectrum of the 10% solution was then carefully integrated (field sweep mode) 10 times and was subdivided into 6 regions with distinct 'valleys' between them. The signals within each region were assigned on the basis of the spectra of the individual mononitrobenzo[b]thiophens (Table 3). It was assumed that the mononitrobenzo[b]thiophens were the only products present and a careful examination of both the 10% and the 2% spectra revealed no signals which did not correspond to them. However, due to the complexity of the spectrum of the mixture, the presence of small amounts (less than ca. 5 mole %) of other materials cannot be excluded. The above procedure enabled us to set up six simultaneous equations and solve them for the percentages of the total signal intensity and hence for the mole percentage of the products. The results are quoted in the text (to the nearest mole %) and the solution of the equations actually gave a small (<2 mole %) negative value for 5-nitrobenzo[b]thiophen as the *expected* signals for this isomer were also included in the setting up of the simultaneous equations. While the reproducibility of the integrals was satisfactory  $(\pm 2\%$  of the peak areas) the results are probably significant to no better than  $\pm 3$  mole % because some of the groups of peaks had small total areas and hence relatively large errors were involved in their determination.

G.l.c.—Three instruments were used: (a) a standard Pye Panchromatograph giving preheating of the argon carriergas and fitted with standard glass tubes, containing the column packing (5 ft. internal diam. ca. 3/16 in.). The detector was of the flame ionisation type and the current from the detector was fed into a Hitachi Perkin-Elmer 159 recorder with sensitivity of 0-2.5 mv; (b) a Perkin-Elmer F.11 gas chromatograph fitted with coiled columns (6 ft. and 3 ft.) with the detector current being fed either into a Honeywell Brown pen recorder with sensitivity 0-1 mv or into the Hitachi Perkin-Elmer recorder; (c) a Pye Argon Chromatograph fitted with standard straight glass tubes (4 ft). There was no preheating of the Argon gas and the detector was the standard Lovelock argon ionisation type, fitted with a <sup>90</sup>Sr source. The pen recorder was the Honeywell Brown recorder with sensitivity 0-10 mv.

Column packings were prepared on D.M.C.S. treated Chromasorb W (Perkin-Elmer) of 100—120 mesh. The coating with stationary phase was achieved by weighing out the required quantity of the desired stationary phase [viz. Versamide (Wilkens Instrument and Research Inc.), Reoplex (Gas Chromatography Ltd.), Silicone polymer SE-30 (Applied Science Laboratories Inc.), Polyethylene **3** R glycol adipate, PEGA, or HI-EFF 8B Silicone (Applied Science Laboratories)], dissolution in an AnalaR solvent, and adding the support to the solution. For the PEGA and Reoplex the solvent was chloroform, for the Versamide it was chloroform : methanol, 80:20, and for the SE-30 and HI-EFF Silicone it was methanol. The solvent was removed by distillation under reduced pressure at  $100^{\circ}$ . Column packings so prepared contained 10% (w/v) Versamide, 5% (w/v) SE-30, 10% (w/v) Reoplex, 10% (w/v) PEGA and 3% (w/v) HI-EFF Silicone.

The glass tubes were filled with the required column packing with repeated gentle tapping. Before any freshly packed column was used for chromatography it was stabilised by heating at ca. 200° for 24 hr. in a slow stream of argon.

Measurements of retention times were made between the first displacement of the recorder pen after the injection and the point corresponding to the peak of the response to the compound concerned. Quantitative analyses of the traces were achieved by the gravimetric method.

Mononitration of Benzo[b]thiophen.—Method A. To a mixture of acetic acid (50 ml.) and fuming nitric acid (12 ml.) maintained at one or other of several different temperatures was added dropwise, with stirring, benzo[b]thiophen (15 g., 0.11 mole) dissolved in acetic acid (15 ml.). After addition was complete stirring was continued and the temperature was held constant for a further 2 hr. The mixture was poured into ice-water and the organic material was extracted into chloroform. After being washed with sodium hydrogen carbonate solution and water, the chloroform solution was dried and the solvent was removed to give the total mixed products.

Analysis by means of  ${}^{1}\text{H}$  n.m.r. spectroscopy was carried out on the product from a run at  $60^{\circ}$  as described above.

Method B. To benzo[b]thiophen (19.6 g.) dissolved in concentrated sulphuric acid (240 ml.) at 0° was added dropwise, with stirring, a solution of potassium nitrate (14.7 g., 1 mole) in concentrated sulphuric acid (240 ml.), the temperature being kept between 0-4°. After addition was complete, stirring was continued for a further hour before the mixture was poured onto crushed ice and the crude product was collected by filtration. It was washed well with water and dried (16 g.). T.l.c. revealed the mixture to contain much polymeric material and unchanged benzo[b]thiophen, with smaller quantities of mono- and di-nitrated benzo[b]thiophens of which 3,4-dinitrobenzo[b]thiophen was the major component. The identity of this last compound was confirmed by its isolation by means of silica column chromatography and direct comparison with an authentic specimen.

Method C. To a well stirred, ice-cooled solution of benzo-[b]thiophen (2 g.) in acetic anhydride (10 ml.) was added dropwise a solution of fuming nitric acid (1 ml., 1.07 mole) in acetic acid (8 ml.). Stirring was continued for 15 min. after addition was complete and the mixture was poured onto ice. T.l.c. of the resulting waxy solid after it had been washed and dried showed, in addition, to base line material two spots corresponding to unchanged benzo[b]thiophen and mononitrated material. A g.l.c. analysis revealed the ratios of the 2- and/or 3- and/or 4-isomers, the 7-isomer, and the 5- and/or 6-isomers to be 85:3:12.

A t.l.c. plate of the waxy solid obtained using a 2 molar proportion in place of a 1 molar proportion of nitric acid revealed the presence, along with base line material, of mono- and dinitro-benzo[b]thiophens. A g.l.c. analysis

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revealed the relative ratios of the mononitro-isomers to be similar to that obtained using the 1 molar proportion.

Attempted Dinitration of Benzo[b]thiophen.—To benzo[b]thiophen (34 g.) in concentrated sulphuric acid (350 ml.) was added with stirring, a solution of potassium nitrate (50-5 g., 2 mole) in concentrated sulphuric acid (100 ml.), the temperature being kept below 4°. After addition was complete (ca. 30 min.) the mixture was left at room temperature for 2 hr. and then poured onto crushed ice. The crystalline mass (24 g.) which formed was collected by filtration. T.l.c. of the crude material revealed one major product of  $R_{\rm F}$  0·32, which on isolation by way of filtration of a chloroform solution of the crude material through silica and crystallisation from methanol proved identical with authentic 3,4,6-trinitrobenzo[b]thiophen prepared as described below.

4-Nitrobenzo[b]thiophen.— 4-Nitrobenzo[b]thiophen-3-carboxylic acid (1.6 g.),<sup>24</sup> redistilled quinoline (30 ml.), and copper bronze powder (1 g.) were heated and stirred in an atmosphere of nitrogen at 170° for 6 hr. The mixture was cooled, chloroform (100 ml.) was added and the insoluble material was filtered off. The filtrate was thoroughly extracted with concentrated hydrochloric acid and washed with water, sodium hydroxide solution (20%), and water, the solution was then dried. Removal of the solvent followed by chromatography of the residue over alumina gave yellow needles eluted with benzene-chloroform (1:1) which had m.p. 83—84° [from light petroleum (b.p. 60— 80°)] (lit.,<sup>4</sup> m.p. 84—85°). There was no m.p. depression on admixture with a specimen prepared by an alternative route.<sup>2</sup>

6-Nitrobenzo[b]thiophen. 6-Nitrobenzo[b]thiophen. 3-carboxylic acid <sup>24</sup> (2.5 g.) was decarboxylated by the same procedure as described above for the 4-nitro-isomer employing redistilled quinoline (50 ml.) and copper bronze powder (1 g.). Yellow needles from ethanol had m.p. 79-80° (lit.,<sup>4</sup> 95-97°) (Found: C, 53.7; H, 3.2. Calc. for C<sub>8</sub>H<sub>5</sub>NO<sub>2</sub>S: C, 53.6; H, 2.8%). A 1:1 mixture with 5-nitrobenzo[b]thiophen melted at 93-110° and 1:3 mixture melted at 100-130°.

7-Nitrobenzo[b]thiophen.— 7-Nitrobenzo[b]thiophen-3-carboxylic acid <sup>24</sup> (0.25 g.) was decarboxylated by the same procedure as described above for the 4-nitro-isomer employing redistilled quinoline (5 ml.) and copper bronze powder (0.15 g.). It was obtained as yellow needles from light petroleum (b.p. 60—80°) and had m.p. 116—117° (lit.,<sup>4</sup> 92—93°) (Found: C, 53.6; H, 2.8. Calc. for  $C_8H_5NO_2S$ : C, 53.6; H, 2.8%).

Nitration of 3-Nitrobenzo[b]thiophen (Ia).-Method A. 3-Nitrobenzo[b]thiophen<sup>22</sup> (4.7 g.) in concentrated sulphuric acid (45 ml.) was nitrated as described by Fries et  $al^2$  with the temperature being kept below 4°. The reaction mixture was poured into water and the total precipitate was filtered off collected and dried (7.1 g.). T.l.c. of the crude material showed the presence of starting material together with at least five other components having  $R_{\rm F}$  values 0.57, 0.51, 0.47, 0.41, 0.32. Column chromatography over silica gel (250 g.) gave all five compounds in pure form. These were identified in serial order of elution as: (i) 3,7-dinitrobenzo[b]thiophen, (ii) 3,6-dinitrobenzo[b]thiophen, (iii) 3,5-dinitrobenzo[b]thiophen, (iv) 3,4-dinitrobenzo[b]thiophen, and (v) 3,4,6-trinitrobenzo[b]thiophen; direct comparison of each compound with a specimen prepared, as described below, confirmed their individual identities.

G.l.c. of the total crude product employing 3% (w/v)

HI-EFF Silicone on Chromasorb W as stationary phase, an argon gas flow of 50 ml./min., and a temperature of  $230^{\circ}$  in the F-11 gas chromatograph gave resolution of the mono- and dinitro-material. Integration of the areas under the peaks gave the ratios of the 3,7-, 3,6-, 3,5-, and 3,4-dinitrobenzo[b]thiophens as 3%, 36%, 23%, and 21%, respectively, with 15% of unchanged 3-nitrobenzo[b]thiophen. Retention times expressed as Kovats retention indices for the four isomers were: 3,7-dinitro-compound 2834-1, 3,6-dinitro-compound 2931-1, 3,5-dinitro-compound 2988-4, and 3,4-dinitro compound 3060-4. In no case could we detect the presence of trinitro-compounds on the g.l.c. traces.

Method B. To an ice-cold mixture of 3-nitrobenzo[b]thiophen (1 g.) in acetic anhydride (8 ml.) under efficient highspeed stirring was added dropwise a solution of fuming nitric acid (0.4 ml., 1.00 mole) in acetic acid (4 ml.). Stirring was maintained for 15 min. after addition was complete and the mixture was then poured onto ice. T.l.c. of the collected solid (1 g.) after it had been washed and dried revealed the presence of mono- and small amounts of di-nitrobenzo[b]thiophens. T.l.c. and g.l.c. analyses of the yellow solid obtained by using a 2 molar proportion in place of a 1 molar proportion of nitric acid revealed the presence of mono- and dinitro-benzo[b]thiophens. The ratios of the 3,6-, 3,5-, 3,4-, and 3,7-dinitro-isomers were 35: 28: 24: 3.

Attempts to nitrate 3-nitrobenzo[b]thiophen with fuming nitric acid in acetic acid at various temperatures were unsuccessful.

3,7-Dinitrobenzo[b]thiophen (III).—7-Nitrobenzo[b]thiophen (20 mg.) was nitrated by the procedure previously employed <sup>7</sup> for the nitration of 5-nitrobenzo[b]thiophen to give 3,7-dinitrobenzo[b]thiophen (12 mg.) m.p. 183—184° (from ethanol) (Found: C, 42.9; H, 2.0;  $C_8H_4N_2O_4S$  requires C, 42.9; H, 1.8%), high resolution mass spectrum: parent peak at m/e 223.98966; calc. for  $C_8H_4N_2O_4^{32}S^+$ , 223.98917.

3,6-Dinitrobenzo[b]thiophen (IV).—6-Nitrobenzo[b]thiophen (17 mg.) on nitration as above gave 3,6-dinitrobenzo-[b]thiophen (10 mg.), m.p. 172—173° (from ethanol) (Found: C, 42·4; H, 2·1.  $C_8H_4N_2O_4S$  requires C, 42·9; H, 1·8%), high resolution mass spectrum: parent peak at m/e223·98923; calc. for  $C_8H_4N_2O_4{}^{32}S^+$ , 223·98917.

3,5-Dinitrobenzo[b]thiophen (V).—Nitration of 5-nitrobenzo[b]thiophen (0.53 g.) as previously described <sup>7</sup> gave 3,5-dinitrobenzo[b]thiophen (0.3 g.), m.p. 169—170° (lit., <sup>7</sup> 171°) (Found: C, 42.9; H, 2.2. Calc. for  $C_8H_4N_2O_4S$ , C, 42.9; H, 1.8%), high resolution mass spectrum: parent peak at m/e 223.98923; calc. for  $C_8H_4N_2O_4^{32}S^+$ , 223.98917.

3,4-Dinitrobenzo[b]thiophen (VI).—Work-up of the product of a separate nitration of 3-nitrobenzo[b]thiophen in the manner described previously <sup>2</sup> gave 3,4-dinitrobenzo-[b]thiophen, m.p. 199—200° (lit.,<sup>2</sup> 199.5°). The same product (10 mg.) was isolated on nitration of 4-nitrobenzo-[b]thiophen (16 mg.) by the procedure previously described <sup>7</sup> for the nitration of 5-nitrobenzo[b]thiophen. High resolution mass spectrum: parent peak at m/e 223.98944; calc. for C<sub>8</sub>H<sub>4</sub>N<sub>2</sub>O<sub>4</sub><sup>32</sup>S<sup>+</sup>, 223.98917.

Treatment of 3,4-dinitrobenzo[b]thiophen (0.2 g.) in ethanol (1.2 ml.) and ammonia  $(d \ 0.880; \ 0.8 \text{ ml.})$  at the b.p. with a rapid stream of hydrogen sulphide for 10 min. gave 4-nitrobenzo[b]thiophen identical in all respects with a specimen prepared by decarboxylation of 4-nitrobenzo[b]thiophen-3-carboxylic acid. 3,4,6-Trinitrobenzo[b]thiophen.—To 3,4-dinitrobenzo[b]thiophen (20 mg.) in concentrated sulphuric acid (0.5 ml.) between 0—5° was added, with stirring, potassium nitrate (30 mg.) in concentrated sulphuric acid (0.5 ml.). The solution was stirred for a further 2—3 hr. and it was then allowed to come to room temperature. The product, 3,4,6-trinitrobenzo[b]thiophen (17 mg.) was obtained by pouring the reaction mixture onto ice and collecting the crystalline mass. It had m.p. 204—205° (from ethanol) (Found: C, 35.7; H, 1.8.  $C_8H_3N_3O_6S$  requires C, 35.7; H, 1.1%). Previous authors erroneously assigned this compound the structure of the 3,4,7-trinitro-isomer <sup>2</sup> and the 3,5,7-trinitro-isomer.<sup>7</sup>

3,6-Dinitrobenzo[b]thiophen (30 mg.) on nitration as above gave an identical product (15 mg.). High-resolution mass spectrum: parent peak at m/e 268·97347; calc. for  $C_8H_3N_3O_6^{32}S^+$ , 268·97425. The <sup>1</sup>H n.m.r. spectrum run in CDCl<sub>3</sub> soln. at *ca.* 2% (w/v) revealed two finely split doublets at 9.03 and 8.88 p.p.m., each showing a splitting of 2.0 Hz with the signal at 8.88 p.p.m. showing further fine

splitting of ca.  $0\cdot 1 - 0\cdot 2$  Hz. These are assignable to 5-H and 7-H while a singlet at 8.85 p.p.m. showing fine splitting of ca.  $0\cdot 1 - 0\cdot 2$  Hz at highest resolution is assigned to 2-H. The absence of splitting assignable <sup>1</sup> to  $J_{2.6}$  rules out the alternative structure 3,5,7-trinitrobenzo[b]thiophen.

3,5,7-Trinitrobenzo[b]thiophen.— 3,5-Dinitrobenzo[b]thiophen (30 mg.) was nitrated as above and the product, 3,5,7-trinitrobenzo[b]thiophen (20 mg.), had m.p.  $202-202 \cdot 5^{\circ}$  (from ethanol).

3,7-Dinitrobenzo[b]thiophen was nitrated to give the same product (Found: C, 35.4; H, 1.2.  $C_8H_3N_3O_6S$  requires C, 35.7; H, 1.1%).

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